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10/599,292	09/25/2006	Adam Liebert	03100324 AA	6589
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WHITHAM, CURTIS & CHRISTOFFERSON & COOK, P.C. 11491 SUNSET HILLS ROAD SUITE 340 RESTON, VA 20190			GUPTA, VANI	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/599,292	Applicant(s) LIEBERT ET AL.
	Examiner VANI GUPTA	Art Unit 3777

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 23 February 2011.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-15 and 17-23 is/are pending in the application.
 - 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-15 and 17-23 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftperson's Patent Drawing Review (PTO-942)
- 3) Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) Notice of Informal Patent Application
- 6) Other: _____

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1 – 10 and 17 – 20 and 22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Claims 1, 5, 17, and 20 contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Particularly, the portion “the detecting step is performed for a time of at least some seconds” is not reasonably conveyed or defined in the disclosure (drawings or specification).

Dependent claims 1 – 4, 6 – 10, 18 - 19, and 22 are rejected for being dependent on claims 1 and 17 and not further clarifying the aforementioned issue(s).

2. Claims 1 – 10 and 17 – 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 5, 17, and 20 are rejected under this paragraph because the phrase “at least some seconds” is a relative phrase which renders the claim indefinite. It is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one

Art Unit: 3777

of ordinary skill in the art would not be reasonably apprised of the scope of the invention (please refer to the first paragraph rejection, above). One of ordinary skill in the art could reasonably assume that this could include as little as one thousandth of a second to one hundred seconds, and therefore does not properly establish the metes and bounds for this claim.

Dependent claims 1 – 4, 6 – 10, 18 - 19, and 22 are rejected for being dependent on claims 1 and 17 and not further clarifying the aforementioned issue(s).

Claim 21 recites the limitation “the reflectance detector” in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1, 4, 7, 8, 11, 14, 17, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Shapiro (US 4,249,825).

Regarding Claim 1, Shapiro suggests a method for detecting a dye bolus injected into the body of a living being, comprising the steps of:

injecting a non-specific (i.e. non-binding) fluorescent dye bolus into the body, the dye bolus having a transit time (col. 1, ll. 49 – 61; col. 3, line 50 - col. 4, line 10; col. 4, ll. 33 - 46); irradiating an optical excitation radiation into a predetermined region of the body the excitation radiation being chosen so as to excite a fluorescence radiation of the non-specific fluorescent dye (col. 1, ll. 52 – 57; col. 2, ll.); and

detecting the fluorescence radiation occurring on a surface of the body (via “ocular image.”

In light of the aforementioned 35 USC 112 second paragraph rejection and for purposes of examination, Examiner interprets wherein the detecting step is performed for a time of at least some seconds to encompass enough time to acquire several optical-based image frames, or at least enough time to monitor “arrival of the dye in regions of interest (col. 4, ll. 1 – 17; col. 7, ll. 3 – 5).

Shapiro suggests also measuring the time between the irradiation of the optical excitation radiation and the occurrence of the fluorescence radiation caused by the excitation radiation thereby determining a flight time of fluorescent photons through a tissue between a location of the dye bolus and the surface of the body (col. 9, line 28 – col. 10, line 64), at multiple times during the transit time of the dye bolus, (“each selected site of fundus”) determining the flight time during the transit of the dye bolus through the tissue and thereby constructing a profile of the photon flight time over the transit time of the dye bolus, the profile being used to evaluate the tissue, the profile including at least some seconds of detection of the dye bolus (col. 8, line 67 – col. 10, line 64).

Regarding Claim 4, Shapiro suggests blocking off the frequency of the excitation radiation by filtering for the detection of the fluorescence radiation (col. 5, ll. 50 – 58).

Regarding Claim 7, Shapiro suggests evaluating detecting fluorescence radiation by assessing the distribution of the measured time of flight photons (see last part of rejection of Claim 1).

Regarding Claim 8, Shapiro suggests the method as claimed in claim 7 wherein an increase of the mean flight time of the fluorescent light is used as an indicator for the start of the detected dye bolus as fluorescence detection is based on blood flow as dye dilutes into blood, and Shapiro is accounting for average blood flow (col. 9, ll. 1 – 26).

Regarding Claim 11, Shapiro discloses a device for detecting a fluorescent dye bolus injected into the body of a living being, comprising:

- a. an optical radiation source for irradiating an excitation radiation into the body, said excitation radiation being chosen so as to excite a fluorescence radiation of the fluorescent dye (col. 2, ll. 45 – 47; see also rejection of Claim 1);
- b. a detection arrangement for detecting a fluorescence radiation of the fluorescent dye (col. 2, ll. 52 – 61; see rejection of Claim 1). For parts a. and b., see also col. 4, line 64 - col. 5, line 66; and
- c. a measurement device (a computer) for detecting a time difference between a time of irradiation of said excitation ad a time of detection of said fluorescence radiation (col. 6, ll. 35 – 36; see also rejection of Claim 1); and
- d. a computer that receives multiple-fluorescence measurements made by the detection arrangement over a time period of at least some seconds (see rejection of part c. for measurement device and rejection of Claim 1).

Regarding Claim 14, Shapiro suggests that the detection arrangement disclosed above comprises an optical filter for blocking off the radiation (col. 5, ll. 50 – 58).

Regarding Claim 17, Sevick discloses a method for detecting a dye bolus within the body of living being, comprising the steps of injecting a fluorescent dye bolus into the body, the

Art Unit: 3777

dye bolus having transit time; irradiating an optical excitation radiation into a predetermined region of the body, the excitation radiation being chosen so as to excite a fluorescence radiation of the fluorescent dye; detecting the fluorescence radiation on the surface of the body, wherein a high frequency modulated light is used as the excitation radiation and the modulation depth and the phase of the fluorescence radiation are determined in order to determine the flight time of fluorescence photons, wherein the detection step is performed for a time of at least some seconds; and at multiple times during the transit time of the dye bolus, determining the flight time during the transit of the dye bolus through the tissue so as to obtain a profile of the photon flight time over the transit time of the dye bolus, the profile being used to evaluate the tissue, the profile including at least some seconds of the dye bolus (please see rejection of claim 1).

Regarding Claim 19, Shapiro suggests the method of claim 1, wherein constructing the profile includes constructing a profile in which the fluorescence photons behave very differently than the reflected light during transit of the dye bolus (col. 9, ll. 11 - 35)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 2 and 12 are rejected under 35 USC 103(a) as being unpatentable over Shapiro as applied to Claim 1 above, in view of Kessler et al. (US 5,610,932).

Regarding claims 2 and 12, Shapiro suggests method and apparatus for detecting a (fluorescent) dye bolus injected into the body of a living being, as explained above.

However, Shapiro does not suggest specifically emitting an excitation radiation from an optical radiation source a short pulse with a pulse width in the picosecond range.

Nonetheless, Kessler et al. (hereinafter Kessler) teaches that it is known in the art to emit a excitation radiation pulse with a pulse width in the picosecond range for fluorescence detection (col. 1, ll. 5 – 19).

Accordingly, it would be obvious to one of ordinary skill in the art, having the teachings of Shapiro and Kessler before one at the time the invention was made, to modify the method of detecting a fluorescing dye bolus of Shapiro with the parameters of the excitation step of Kessler to so that one could detect fluorescence with greater flexibility, as explained by Kessler.

5. Claims 3, 5, 6, 13, 15, and 21 – 23 are rejected under 35 USC 103(a) as being unpatentable over Shapiro as applied to claims 1, 11, and 17 above, further in view of Folestad et al. (US 6,794,670 B1).

Regarding Claim 3, Shapiro teaches each and every limitation of the claim, as discussed above in reference to claim 1.

However, Shapiro differs from Claim 3 in that Shapiro does not teach the method as claimed, wherein the time course of the fluorescence radiation is determined with a nanosecond or picosecond time resolution.

Nonetheless, Folestad et al. (hereinafter Folestad) suggests that time course of the fluorescence radiation may be determined with nanosecond time resolution (col. 14, ll. 35 – 37).

Accordingly, it would be obvious to one of ordinary skill in the art, having the teachings of Shapiro and Floestad before one at the time the invention was made, to modify method of detecting a fluorescing dye bolus of Shapiro with a step of detecting the excitation radiation diffusely reflected from the body simultaneously of Folestad so that one could accomplish both tasks in time-resolved manner using one component of the same apparatus, which would take up less resources (cost, infrastructure, material, etc.).

Regarding claim 5, Folestad discusses detecting the radiation reflected from the sample as well as the diffusely backscattered radiation by a single lens (*fig. 1b, L4'*); and accomplishing it in a time-resolved manner (col. 6, ll. 35 – 54).

Regarding Claim 6, please refer to teachings of Folestad as described in the rejection of Claim 5.

Regarding Claim 13, Folestad suggests that the detection arrangement disclosed above is designed to detect the time course of fluorescence radiation with nanosecond or picosecond time resolution (*fig. 3b*).

Regarding Claim 15, Shapiro in view of Folestad suggests a detection arrangement comprising at least one detector branch for detection of excitation radiation diffusely reflected by the body in said region. With respect to providing an additional detector branch for accomplishing the same, mere duplication of parts such as a detector branch are well known within the ordinary skill in the art, and unless a new unexpected results is produced by providing additional detection components, this feature has no patentable weight. See *In re Harza*, 274 F.2d 669, 124 USPQ 378 (CCPA 1960). It would *prima facie* obvious to modify Shapiro in view

Folestad to include additional detection components so that one may maximize on operation of the apparatus and obtain additional information.

Regarding Claim 21, with respect to the device of claim 11, including no more than two detectors including the fluorescence detection arrangement and the reflectance detector, Applicant should note that provide no more than a specific number of similarly performing parts would have been obvious to one having ordinary skill in the art at the time of the invention was made, since it has been held that forming in one piece an article, which has formerly been formed in two pieces and put together involves only routine skill in the art. See Howard v. Detroit Stove Works, 150 U.S. 164 (1893).

Regarding Claim 22, please refer to the rejection of claim 5 above.

Regarding Claim 23, Shapiro in view of Folestad suggests the device of claim 11, further including a detector that carries out reflection measurement, and wherein the computer also is capable of receiving multiple reflection measurements made by the detector over the time period (refer to rejection of claim 5).

6. Claim 9 is rejected under 35 USC 103(a) as being unpatentable over Shapiro as applied to Claim 1 above, in view of Boas (US 6,516,214).

Regarding Claim 9, Shapiro suggests method for detecting a (fluorescent) dye bolus injected into the body of a living being, as explained above.

However, Shapiro does not suggest specifically irradiating the region by said excitation radiation at the head and examining the brain.

Nonetheless, Boas teaches administering a dye bolus into the blood stream of a patient, directing light into the brain of the subject, and detecting light emitted from the brain over time at a detection location (col. 2, ll. 4 – 26).

Accordingly, it would be obvious to one skilled in the art, having the teachings of Shapiro and Boas before one at the time of the invention was made, to modify the method for detecting a fluorescing dye bolus of Shapiro to include the step of monitoring the brain region of Boas for additional diagnostic information.

7. Claim 10 is rejected under 35 USC 103(a) as being unpatentable over Shapiro as applied to Claim 1 above, in view of Zhao et al. (US 2003/0031628 A1).

Regarding Claim 10, Shapiro suggests method and apparatus for detecting a (fluorescent) dye bolus injected into the body of a living being, as explained above.

However, Shapiro does not suggest specifically irradiating a lungs area by said excitation radiation.

Nonetheless, Zhao et al. describes an experimentation involving first injecting mice suffering from tumors with dye bolus, and then directing optical excitation radiation into the area of the lungs. The tumor areas fluoresced as a result of the application of excitation radiation (para. [0045]).

It would be obvious to one of ordinary skill in the art, having the teachings of Shapiro and Zhao before one at the time of the invention was made, to modify the method for detecting a fluorescing dye bolus of Shapiro to include the step of monitoring the lungs region to obtain additional diagnostic information.

8. Claims 18 and 20 are rejected under 35 USC 103(a) as being unpatentable over Shapiro as in view of Folestad et al. (US 6,794,670 B1).

Regarding Claim 20, Shapiro in view of Folestad suggests a method for detecting a dye bolus injected into the body of a living being, comprising the steps of: injecting a non-specific fluorescent dye bolus into the body; irradiating an optical excitation radiation into a predetermined region of the body the excitation radiation being chosen so as to excite a fluorescence radiation of the non-specific fluorescent dye; detecting the fluorescence radiation occurring on a surface of the body, wherein the detecting step is performed for a time of at least some seconds (see rejection of claim 1); simultaneously and in parallel to the step of detecting the fluorescence radiation, also detecting excitation radiation diffusely reflected from the body (see rejection of claim 5); receiving results of the fluorescence detecting and the reflection detecting in a computer (see rejection of Claim 11), and constructing a profile in which is plotted, against time, two curves including a fluorescence curve (see Shapiro – col. 9, line 1 – col. 10, line 64) and a separate reflectance curve (Folestad: **figs. 3a, 3b**).

Regarding claim 18, Shapiro in view of Folestad teaches each and every limitation of the claim, as discussed above in reference to claim 1.

However, Shapiro in view of Folestad differs from Claim 18 in that Shapiro does not teach the method of claim I, including constructing a profile in a form of a graph that shows two plots as a function of time, including a plot for fluorescence and a plot for reflection, wherein the graph is for about 240 seconds wherein an injection time of the bolus occurs between 0 and 60 seconds.

Nonetheless, as it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide a graph that plots multiple values such as fluorescence and reflection with a range of 0 to 240 seconds limited by an injection time of the bolus between 0 and 60 seconds, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only ordinary skill in the art or routine experimentation, and does not receive any patentable weight. Furthermore, Examiner has noted that the disclosure of the present application has not provided a criticality or provides an advantage, is used for a particular purpose, or solves a stated problem, for plotting a graph for these two variables within these parameters. See *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

One of ordinary skill in the art, furthermore, would have expected the teachings of Shapiro and Folestad, and applicant's invention, to perform equally well with either the range taught by Shapiro in view of Folestad or the claimed range for time because both ranges would provide one of ordinary skill of the art enough information about fluorescence and reflection within any time of injection of dye bolus.

Therefore, it would have been *prima facie* obvious to modify Shapiro in view of Folestad to obtain the invention as specified in claim 1 because such a modification would have been considered a mere design consideration which fails to patentably distinguish over the prior art of Shapiro in view of Folestad.

Response to Arguments

9. Applicant's arguments, see pp. 7 – 9 are, filed February 23, 2010, with respect to the rejection(s) of claim(s) 1 – 15 and 17 – 23 under Sevick-Muraca (US 7,328,059) have been fully

considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Shapiro (US 4,249,825). Applicant's arguments are moot in view of these new ground(s) of rejection.

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to VANI GUPTA whose telephone number is (571)270-5042. The examiner can normally be reached on Monday - Thursday (8:30 am - 6:00 pm; EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert (Tse) Chen can be reached on 571-272-3672. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 3777

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/V. G./
Examiner, Art Unit 3777

/Tse Chen/
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